from ether–hexane giving 80 mg. of white crystals of α,α-dicyano-α-chloro-*p*-toluoyl cyanide, m.p. 78–83°. The infrared spectrum of the product shows absorption at 3100 (Ar–H), 2225 (nitrile of acyl cyanide), 1695 (carbonyl of acyl cyanide), 1612 and 1503 (aromatic) and 816 cm.$^{-1}$ (1,4-disubstituted benzene).

Anal. Calcd. for $C_{11}H_4N_3OCl$: C, 57.53; H, 1.76; N, 18.30; Cl, 15.44. Found: C, 57.99; H, 1.93; N, 18.45; Cl, 15.02.

Terephthaloyl Cyanide.—A suspension of 20.5 g. of TCNQ in 200 ml. of acetonitrile was cooled to 0° under a nitrogen atmosphere. Nitrogen dioxide (10.9 g.) was added to the stirred mixture. The mixture was stirred for 16 hours during which time it became homogeneous. The solvent was removed under reduced pressure leaving a green oil as a residue. The oil evolved NO_2 on standing at room temperature and more rapidly on addition of a solvent. Decomposition of the oil is effected more advantageously by heating at 130° under vacuum in a sublimation apparatus. A near-white solid is deposited on the cold finger. Recrystallization from benzene gave crude terephthaloyl cyanide (13.8 g., 75%), m.p. 140–142°. Sublimation gave material of m.p. 148–149°.

Anal. Calcd. for $C_{10}H_4N_2O_2$: C, 65.22; H, 2.19; N, 15.22. Found: C, 65.89; H, 2.39; N, 14.76.

Upon standing the nitrogen content of the sample decreased, probably as a result of hydrolysis. The infrared spectrum of terephthaloyl cyanide is quite simple. It shows absorption at 2230 cm.$^{-1}$ (nitrile) and 1690 cm.$^{-1}$ (carbonyl). The aromatic absorption at 1500 cm.$^{-1}$ is moderate, but that at 1600 cm.$^{-1}$ is very weak. There is no absorption in the region 800–860 cm.$^{-1}$ normally cited for *p*-substituted aromatics, but this has also been noted previously for dimethyl terephthalate. Terephthaloyl cyanide does absorb at 875 cm.$^{-1}$, but this absorption is not as intense as that customarily due to a *p*-substituted aromatic compound.

Terephthaloyl cyanide was warmed in methanol solution and the odor of hydrogen cyanide was observed. Evaporation of the methanol left a solid residue which was sublimed to give dimethyl terephthalate, m.p. 142.5–143.5°.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE MASSACHUSETTS INSTITUTE OF TECHNOLOGY, CAMBRIDGE, MASS., AND THE RESEARCH LABORATORIES OF CHAS. PFIZER AND CO., INC., GROTON, CONN.]

Structure and Synthesis of Flavocarpine

BY G. BÜCHI, R. E. MANNING[1] AND F. A. HOCHSTEIN

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The stem bark of *Pleiocarpa mutica* Benth. contains a yellow zwitterionic substance which we have named flavocarpine. Decarboxylation gave flavopereirine. The position of the carboxyl group was established from a study of the ultraviolet, infrared, mass and nuclear magnetic resonance spectra of a methyl ester prepared by reduction of flavocarpine methyl ester hydrochloride with sodium borohydride. The structure proposed was confirmed by a total synthesis.

Preliminary chemical analyses of *Pleiocarpa tubicina* Stapf[2] and *Pleiocarpa mutica* Benth.[3] (*Apocyanaceae*) revealed the presence of alkaloids and crude extracts of both plants were reported to exhibit considerable hypotensive activity.[2,4] A systematic search for alkaloids of *P. mutica* Benth. was initiated in several laboratories and the isolation of new indole bases has already been announced.[5–7]

In the present paper we outline our work on the isolation, structure elucidation and synthesis of a new alkaloid, m.p. 307° dec., $[\alpha]_D$ 0°, which we have isolated from the stem bark of *P. mutica* Benth. in 0.0005% yield. The most striking property of this substance is its brilliant yellow color and we have named it "flavocarpine" accordingly. Combustion analyses gave erratic results and the correct empirical formula ($C_{18}H_{14}N_2O_2$) had to be deduced from the composition of transformation products. The infrared spectrum posessed a broad carbonyl band at 1595 cm.$^{-1}$ ascribable to a carboxylate anion. This finding coupled with the extreme insolubility in common organic solvents indicated the presence of a zwitterionic structure. Flavocarpine exhibits complex ultraviolet light absorption (see Experimental) which is *p*H dependent. When measured in dilute hydrochloric acid the spectrum showed a vague resemblance to those of 7H-pyrido[2,3-c]carbazole (8)[8] and 7H-pyrido[4,3-c]carbazole (9)[9] in acid solution, but it was very similar to that of flavopereirine perchlorate.[10,11] The nuclear magnetic resonance spectrum[12] of the natural product in trifluoroacetic acid solution was even more revealing and the only bands appearing at field strengths above 2τ were a quartet centered at 6.58τ corresponding in intensity to two protons and a triplet centered at 8.45τ with an area of three protons. Consequently, five hydrogens are contained in an ethyl group while all other protons are attached to the aromatic system. In summary, the physical measurements discussed indicated that flavocarpine is a C- or N-ethylpyridocarbazolecarboxylic acid or, preferably, an ethyl-indolo[2,3,-a]pyridocolinecarboxylic acid. Reduction of N-alkylpyridocarbazole salts with sodium borohydride affords carbazoles[13] while reduction of indolopyridocoline salts with the same reagent furnishes derivatives with indole chromophores.[14] We have used this diagnostic test to ascertain the aromatic portion in the molecule.

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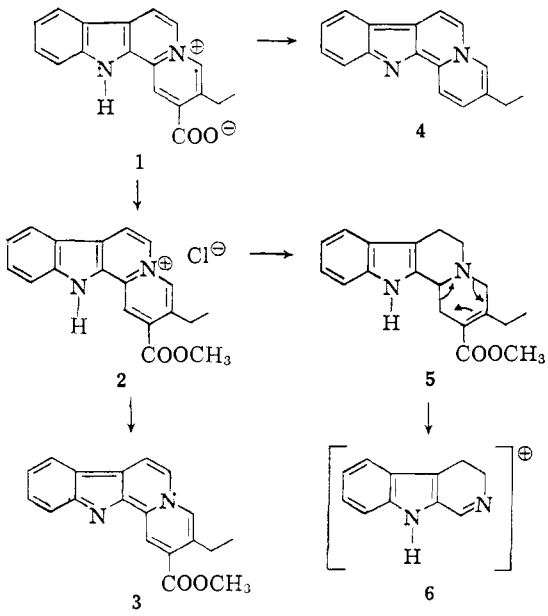
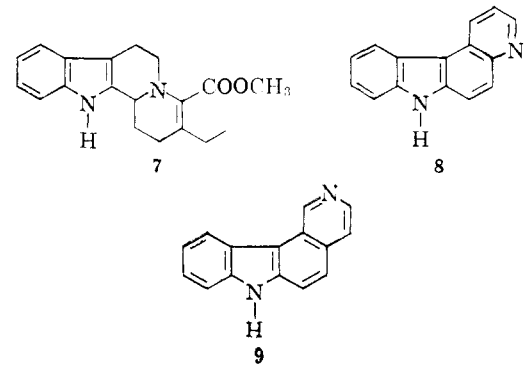
Treatment of flavocarpine(**1**) with hydrogen chloride in methanol solution gave a yellow methyl ester hydrochloride (**2**) which was characterized further by the red methyl ester **3** ($\nu_{max.}$ 1720 cm.$^{-1}$). On reduction with sodium borohydride **2** was transformed smoothly to a basic compound (**5**) with an indole chromophore and infrared peaks at 3480 (NH) and 1705 cm.$^{-1}$ (α,β-unsaturated ester). The presence of an indolo[2,3-a]pyridocoline nucleus was established rigorously by decarboxylation of flavocarpine (**1**) to flavopereirine (**4**).[10,15]

Structure **1** for flavocarpine seemed most reasonable on biogenetic grounds and verification of this assignment was provided by the nuclear magnetic resonance and mass spectra of the reduced methyl ester **5**. The former showed well defined peaks at 2.05 (NH), 2.8 (multiplet, 4H, aromatic protons), 6.22 (OCH_3) and 8.88τ (triplet, CH_3-CH_2-). There were no bands in the 3–6τ region corresponding to vinylic protons and the double bond conjugated with the ester function consequently is tetrasubstituted. A mass spectrum[16] of **5** exhibited a molecular ion peak at mass 310 demanding a molecular composition of $C_{19}H_{22}N_2O_2$. Furthermore the most intense peak in the spectrum corresponded to mass 170 attributable to a fragment (**6**) arising from a retro-Diels–Alder reaction.[17] Such a fragmentation is not possible with the alternate structure (**7**) which is excluded also by the ultraviolet light absorption of the reduced ester. Structure **1** then represents flavocarpine and we have confirmed this assignment by a total synthesis.



The most expedient method of general applicability for the synthesis of 12-H-indolo[2,3,-a]-pyridocolinium salts proceeds through their dihydro compounds (*e.g.*, **17**) available by direct condensation of 3-(2-bromoethyl)-indoles with 2-chloropyridines.[18] To follow this synthetic program we had to prepare 2-chloro-5-ethyl-pyridine-4-carboxylic acid or a suitable derivative thereof. The known 3-ethylpyridine-1-oxide[19](**10**) was alkylated with methyl iodide and the resulting O-methyl iodide (**11**) converted to 3-ethyl-4-cyanopyridine (**12**) by treatment with potassium cyanide.[20] That the cyano group had indeed entered the 4-position was ascertained in two ways: (a) The exceedingly simple nuclear magnetic resonance spectrum (in CCl_4) possessed peaks at 1.35 (1 H, singlet), 1.42 (1 H, doublet J 5 c./s.), 2.53 (1 H, doublet, J 5 c./s.), 7.09 (2 H, quartet, J 7 c./s.) and 8.63τ (3 H, triplet, J 7 c./s.). It is compatible only with structure **12** because **18** should not exhibit a one-proton singlet and the coupling constant between the β- and γ-protons in **19** should be larger than 7 c./s.[21] (b) Wolff–Kishner reduction of 4-acetyl-3-ethylpyridine prepared by condensation of **12** with methylmagnesium iodide afforded 3,4-diethylpyridine identified as the picrate.[22] When **12** was subjected to the action of hydrogen peroxide in acetic acid solution the desired N-oxide **13**[23] was produced in essentially quantitative yield. It was transformed further to an equal mixture of the anticipated chloropyridines **14** and **15** by treatment with phosphorus oxychloride in hot chloroform.[24] If attack by chloride ion in the intermediate **20** occurs perpendicularly to the plane of the pyridine ring, steric interference by the ethyl group should be minimal and the formation of both chloropyridines (**21**, arrows) in approximately equal proportions can be rationalized. In agreement with structure **14** the nuclear magnetic resonance spectrum (in CCl_4) of the lower boiling isomer featured the peaks: doublet 1.64 (1 H, J 5 c./s.), doublet 2.57 (1 H, J 5 c./s.), quartet 6.96 (2 H, J 8 c./s.) and triplet 8.69τ (3 H, J 8 c./s.). The other isomer (**15**) showed bands (in CCl_4) at 1.6 (1 H), 2.5



(15) We are indebted to Professor H. Rapoport for a sample of natural flavopereirine.

(16) We wish to thank Professor K. Biemann and Dr. W. Vetter for this spectrum and its interpretation. It was measured on a CEC 21-103C spectrometer equipped with a heated inlet system (135°) using an ionization potential of 70 v.

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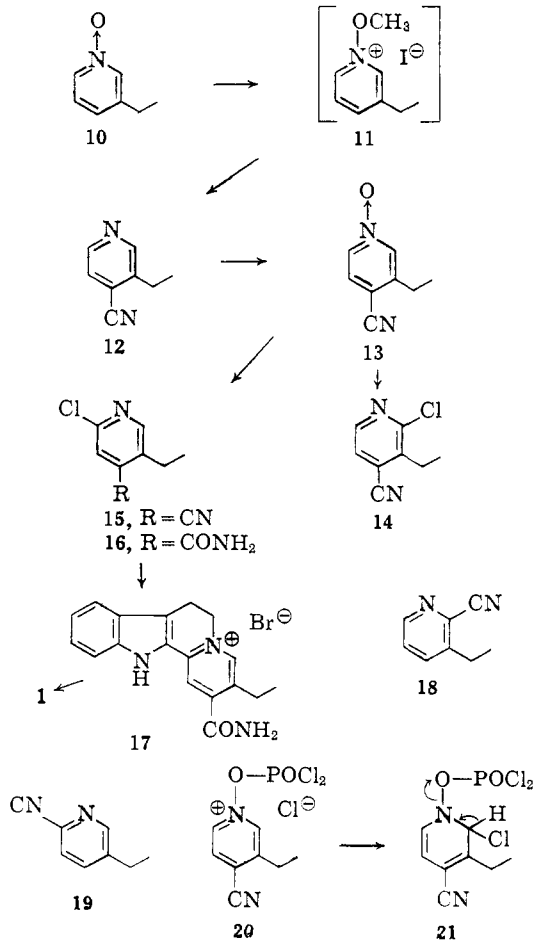
(23) The conversion of 3-ethylpyridine-1-oxide to 4-cyano-3-ethylpyridine-1-oxide was first accomplished by J. Powers of this Laboratory (M.I.T.).

(24) Method of J. Suzuki, *Pharm. Bull. (Japan)*, **5**, 78 (1957).

(1 H), quartet 7.11 (2 H, J 7 c./s.) and triplet 8.63τ (3 H, J 7 c./s.).

Although a suitably substituted pyridine was now available for the final condensation, we decided to use the crystalline amide **16** prepared by the action of hydrogen peroxide on crude **15** rather than the liquid nitrile **15** which was separable from its isomer only by careful fractional distillation. Condensation of the amide **16** with 3-(2-bromoethyl)-indole in hot dioxane furnished a crystalline, red bromide (**17**) whose ultraviolet absorption curve ha d a shape identical with that of a model compound (**17** without carboxamido group)[11] but all four maxima in **17** were displaced to longer wave lengths by approximately 5 mμ. Dehydrogenation of **17** was effected with tetrachloro-*o*-benzoquinone[11] and the resulting amide converted directly to flavocarpine hydrochloride (**2**) by hydrolysis with aqueous hydrochloric acid. The ultraviolet spectra of the synthetic hydrochloride in acid and basic solutions were identical with those of flavocarpine hydrochloride (**2**) and infrared spectra of the two samples in Nujol suspension were very similar but not identical. We attribute the difference to instability of the hydrochloride which loses hydrochloric acid at room temperature. The synthetic hydrochloride was then converted to the amino acid by ion exchange; the infrared and ultraviolet spectra of the synthetic material were identical in all details with those of flavocarpine (**1**) from *P. mutica* Benth. and mixture melting points were not depressed.



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Experimental[25]

Isolation of Flavocarpine (1).—The methanolic extracts of 100 kg. of *Pleiocarpa mutica* stem bark were concentrated to 50% solids (about 20 liters) and dissolved in 5 volumes of 5% aqueous acetic acid. A major portion of the alkaloids was then extracted with chloroform, first at *p*H 4, then at *p*H 10. The remaining aqueous phase, which still gave a strong Mayer test, was extracted 3 times with an equal volume of 1-butanol. The butanol extracts were concentrated to dryness to yield 3 kg. of solids. These solids were subsequently dissolved in 4 l. of 50% acetic acid, diluted to 20 l. and filtered from about 100 g. of insoluble material; 12 l. of saturated aqueous picric acid was added to the filtrate, until no further precipitate formed. The amorphous, yellow-brown picrate, 275 g., was filtered, dried, dissolved in 30 l. of hot methanol, and filtered from about 50 g. of dark brown insoluble residues. The methanol solution was passed over a column containing 2 l. of Amberlite IR-45 resin on the acetate cycle. (Amberlite IR-45 resin is a weakly basic anion exchange resin made by Rohm and Haas.) The column eluate, containing 165 g. of crude alkaloid acetate, was concentrated to dryness, dissolved in 1200 ml. of 15% aqueous acetic acid and submitted to a 10-transfer countercurrent distribution *vs.* 1800 ml. of 9:1 1-butanol–hexane. The contents of each funnel were concentrated to dryness *in vacuo* separately to yield in funnels 0, 1, 2 and 3, 7, 11, 14 and 21 g. of solids. These were dissolved separately in 4 ml. of methanol per g. of solids, held at 0° overnight, and the crystalline product separated by filtration. The contents of funnels 0 and 1 yielded 650 mg. of crude crystalline alkaloid as hexagonal plates. Funnels 2 and 3 yielded smaller amounts of somewhat cruder product. Recrystallization of the crude product from 200 ml. of boiling glacial acetic acid per gram yielded about 500 mg. of recrystallized alkaloid, m.p. 307–308° dec. (evac. capillary), yield 0.0005%, $[\alpha]_D$ = 0 (c 1.52 in HCl, MeOH, H_2O). The alkaloid is slightly soluble in hot 1 N hydrochloric acid, 5% sodium hydroxide, hot glacial acetic acid and hot dioxane. It is insoluble in water, methanol, ethyl acetate, dimethylformamide, toluene, pyridine and chloroform; λ_{max}^{EtOH} 223, 242, 250, 291, 351 and 389 mμ (ϵ 40,800, 48,600, 51,200, 23,000, 23,500 and 22,000, resp.), $\lambda_{max}^{0.01\ N\ HCl}$ 230, 246, 298, 333, 371 and 400 mμ (ϵ 29,900, 32,300, 16,900, 11,600, 13,600 and 12,700, resp.), $\lambda_{max}^{0.01\ N\ NaOH}$ 233, 243, 258, 289, 316, 362 and 438 mμ (ϵ 29,500, 28,900, 24,700, 31,000, 13,700, 20,600 and 7,850, resp.); ν_{max}^{KBr} 1630, 1596, 1525, 1480, 1405, 1375, 1360, 1220, 1190, 1085, 800, 745 cm.$^{-1}$. For analysis a sample was dried to constant weight at 100° (0.02 mm.).

Anal. Calcd. for $C_{18}H_{14}N_2O_2$: C, 74.47; H, 4.86; N, 9.65. Found: C, 74.14; H, 4.86; N, 9.67.

Flavocarpine Hydrochloride.—Flavocarpine (100 mg.) was dissolved in 7 ml. of 1 N hydrochloric acid on a steam-bath. The fine yellow needles, which separated on cooling, were recrystallized three times from 0.5 N hydrochloric acid and the product, m.p. 301–302° (dec., evacuated capillary) (80 mg.), was dried at 100° (0.01 mm.) for 1 hour.

Anal. Calcd. for $C_{18}H_{14}N_2O_2$·HCl: C, 66.1; H, 4.6; N, 8.6; Cl, 10.9. Found: C, 67.05; H, 5.33; N, 7.43; Cl, 5.71.

Apparently, hydrochloric acid was eliminated on drying.

Flavocarpine Methyl Ester Hydrochloride (2).—A slow stream of gaseous hydrogen chloride was passed over a

(25) Melting points, unless specified otherwise, were observed on a hot-stage and are corrected for stem exposure. Boiling points are uncorrected. Analyses were performed by Mr. W. Egger, Scandinavian Microanalytical Laboratory, Copenhagen. Ultraviolet spectra were measured on a Cary recording spectrophotometer, model II, and infrared spectra were taken on a Perkin-Elmer recording spectrophotometer, model 21, with sodium chloride prism. The listings of infrared bands include those which are relevant to the structural arguments and other bands of medium and high intensity. Woelm alumina was used as chromatographic adsorbent and its activity was checked by the method of Brockmann (H. Brockmann and H. Schodder, *Ber.*, **74**, 73 (1941)).

stirred suspension of flavocarpine (500 mg.) in absolute methanol (40 ml.). The solid material dissolved, the solution became hot and was heated subsequently with stirring under a slow stream of hydrogen chloride for 1 hour, during which time yellow needles precipitated. The mixture was allowed to cool under a stream of hydrogen chloride gas, the flask stoppered and allowed to stand for 0.5 hour. Crystals which deposited were collected by filtration, washed with ether and dried *in vacuo* at room temperature to yield 500 mg. of product, m.p. 295–296° dec. (evac. capillary).

Flavocarpine Methyl Ester (3).—A solution of flavocarpine methyl ester hydrochloride (200 mg.) in methanol–water was treated with sodium carbonate solution and extracted with chloroform. The dark-red chloroform layer was washed with water, dried (sodium sulfate) and evaporated to yield a crystalline residue. Two recrystallizations from ethanol yielded pure flavocarpine methyl ester as red needles, m.p. 152–154°, $[\alpha]D$ 0° (*c* 1.17 in $CHCl_3$); λ_{max}^{EtOH} 230, 246, 298, 330 and 375 mμ (ε 29,500, 30,300, 17,400. 10,600 and 13,000, resp.); $\lambda_{max}^{0.01\ N\ HCl}$ 230, 247, 300, 335 and 375 mμ (ε 29,400, 31,100, 17,000, 10,750 and 12,850, resp.); $\lambda_{max}^{0.01\ N\ NaOH}$ 234, 242, 258, 290, 315, 370 and 460 mμ (ε 26,900, 26,800, 20,100, 27,600, 13,400, 18,350 and 4,760 resp.); $\nu_{max}^{CHCl_3}$ 2960, 1720, 1615, 1475, 1405, 1342, 1300, 1250, 1180, 1150, 1115, 855 $cm.^{-1}$.

Anal. Calcd. for $C_{19}H_{16}N_2O_2$: C, 74.98; H, 5.30; N, 9.21. Found: C, 70.74; H, 5.55; N, 7.73.

Sodium Borohydride Reduction of Flavocarpine Methyl Ester Hydrochloride (2).—Sodium borohydride (280 mg.) was added to a solution of flavocarpine methyl ester hydrochloride (200 mg.) in absolute methanol (13 ml.). The solution was heated under reflux for 1 hour, concentrated to about 2 ml., diluted with water and extracted with chloroform. The organic phase was washed with water, dried (sodium sulfate) and evaporated to yield an oil which crystallized. This residue was dissolved in methylene chloride solution and filtered through alumina (activity III) and recrystallized several times from methylene chloride–ether. A solution of this material was then filtered again through alumina (activity III) and the residue obtained by evaporation recrystallized from ethyl acetate–hexane to yield 68 mg. of pure product, m.p. 167–168.5°; λ_{max}^{EtOH} 225, 283 and 290 mμ (ε 47,800, 8,270 and 6,900, resp.); $\nu_{max}^{CHCl_3}$ 3480, 2920, 1705, 1642, 1501, 1453, 1437, 1358, 1322, 1312, 1275, 1240, 1165, 1090, 1070 $cm.^{-1}$.

Anal. Calcd. for $C_{19}H_{22}N_2O_2$: C, 73.52; H, 7.14; N, 9.03. Found: C, 73.26; H, 7.23; N, 8.93.

Decarboxylation of Flavocarpine (1) to Flavopereirine (4).—Copper powder (50 mg.) and freshly prepared brass filings (100 mg.) were added to a suspension of flavocarpine (50 mg.) in quinoline (2.5 ml.). The mixture was heated under reflux for 20 minutes in an atmosphere of nitrogen. Quinoline was removed by steam distillation under reduced pressure and the residue extracted with benzene and methylene chloride. The solvent extract was distilled twice at 200° (0.01 mm.) to furnish an orange oil (11 mg.). Recrystallization from acetone yielded pure flavopereirine, m.p. 205–208°, pure and mixed with an authentic specimen, m.p. 204–207°. An infrared spectrum was identical with that of authentic flavopereirine. A portion was converted to the perchlorate by treatment with perchloric acid in methanol. Recrystallization from the same solvent gave yellow needles, m.p. 309–311°, pure and mixed with an authentic sample, m.p. 308–310°.

4-Cyano-3-ethylpyridine (12).—A mixture of 3-ethylpyridine-1-oxide (**10**) (95 g.) and 150 ml. of methyl iodide was allowed to stand overnight. The crystalline precipitate (**11**) was collected by filtration and the filtrate diluted with a little ether and extracted with water. The above crystalline precipitate was dissolved in the aqueous extract and diluted with water to 400 ml. Dioxane (500 ml.) and potassium cyanide (140 g.) were added and the mixture was stirred at room temperature for 2 hr. The solution was then extracted with chloroform and the extracts washed with water, dried (magnesium sulfate) and evaporated. Distillation of the residue yielded 68 g. of crude cyanopyridines and 25 g. of 3-ethylpyridine-1-oxide. The cyanopyridines were separated by fractional distillation through a spinning band column at 100° (12 mm.). The first fraction (37 g.) was pure 4-cyano-3-ethylpyridine; λ_{max}^{EtOH} 215, 224, 283 mμ (ε 8,150, 6,700 and 3,800, resp.); ν_{max}^{neat} 2260, 1590, 1550, 1490, 1465, 1410, 1380, 1310, 1230, 1205, 1190, 1070, 970, 935, 840, 825, 795, 760, 732 $cm.^{-1}$.

Anal. Calcd. for $C_8H_8N_2$: C, 72.20; H, 6.10; N, 21.20. Found: C, 72.43; H, 6.06; N, 21.03.

3,4-Diethylpyridine.—A solution of 1 g. of 4-cyano-3-ethylpyridine (**12**) in ether was added to an ether solution of the Grignard reagent made from 0.38 g. of magnesium and excess methyl iodide. After several hours at room temperature, 20 ml. of ammonium chloride solution was added to the reaction mixture and the resulting solution extracted with ether. The ether was removed on the steam-bath, the 4-acetyl-3-ethylpyridine distilled and then added to a mixture of 50 ml. of diethylene glycol, 1 g. of 60% hydrazine and 1 g. of potassium hydroxide. This solution was allowed to reflux overnight, the temperature rising to 170°. The reaction mixture was then cooled, diluted with water and extracted with ether to give crude diethyl-pyridine. The picrate after recrystallization from ethanol had m.p. 136.5–138.5° (lit. 140.1°[22a] and 137°).[22b]

4-Cyano-3-ethylpyridine-1-oxide (13).—A mixture of 4-cyano-3-ethylpyridine (**12**) (30 g.), 30% hydrogen peroxide (100 ml.) and glacial acetic acid (250 ml.) was heated on a steam-bath for 18 hr., diluted with 500 ml. of water and evaporated *in vacuo* to 250 ml. Water (500 ml.) was added and the solution concentrated again to about 250 ml. The residue was dissolved in chloroform and treated with a paste of potassium carbonate. The aqueous phase was extracted twice with chloroform, the combined extracts dried and the solvent removed. The residue was crystallized from ethyl acetate to give 28 g. of oxide, m.p. 104–105°, λ_{max}^{EtOH} 230 and 292 mμ (ε 14,550 and 18,200, resp.).

Anal. Calcd. for $C_8H_8N_2O$: C, 64.92; H, 5.45; N, 18.93. Found: C, 64.72; H, 5.20; N, 18.74.

2-Chloro-4-cyano-3-ethylpyridine (14) and 2-Chloro-4-cyano-5-ethylpyridine (15).—A mixture of 4-cyano-3-ethylpyridine-1-oxide (**13**) (25 g.), chloroform (60 ml.) and phosphorus oxychloride (60 ml.) was refluxed for 5 hr., cooled and poured on crushed ice. The aqueous layer was rendered alkaline with sodium carbonate and steam distilled. Extraction of the distillate yielded about 1 g. of **14** and **15**. The chloroform layer was treated with excess sodium carbonate, washed with water, dried (magnesium sulfate) and distilled to give 14 g. of a mixture of **14** and **15** and 2–3 g. of 4-cyano-3-ethylpyridine-N-oxide. The pyridine mixture (15 g.) was fractionally distilled to give a lower-boiling fraction (4.4 g., *ca.* 90% pure as judged from gas–liquid partition chromatography) of 2-chloro-4-cyano-3-ethylpyridine, a middle fraction which was a mixture and a higher-boiling fraction (4.3 g. *ca.* 90% pure) of 2-chloro-4-cyano-5-ethylpyridine. Each fraction was redistilled to give a pure sample.

2-Chloro-4-cyano-3-ethylpyridine (14), ν_{max}^{neat} 2240, 1580, 1550, 1470, 1450, 1390, 1320, 1280, 1240, 1200, 1170, 1090, 1060, 970, 895, 850, 805, 780, 770, 755 $cm.^{-1}$. *Anal.* Calcd. for $C_8H_7N_2Cl$: C, 57.67; H, 4.24; N, 16.82. Found: C, 58.00; H, 4.34; N, 16.66.

2-Chloro-4-cyano-5-ethylpyridine (15), ν_{max}^{neat} 2240, 1580, 1540, 1460, 1380, 1340, 1320, 1295, 1250, 1220, 1205, 1165, 1090, 1060, 965, 930, 890, 870, 790, 755, 740 $cm.^{-1}$. *Anal.* Calcd. for $C_8H_7N_2Cl$: C, 57.67; H, 4.24; N, 16.82. Found: C, 57.79; H, 4.32; N, 16.60.

4-Carboxamido-2-chloro-5-ethylpyridine (16).—A solution of 2-chloro-4-cyano-5-ethylpyridine (**15**) (600 mg.), methanol (8 ml.), 20% aqueous sodium hydroxide solution (0.8 ml.) and 30% hydrogen peroxide (1.2 ml.) was allowed to stand overnight at room temperature. The mixture, which had crystallized partly, was diluted with water and the crystals collected. Recrystallization from acetone–chloroform–ether yielded 540 mg. of product, m.p. 190–191°, λ_{max}^{EtOH} 272 mμ (ε 3,090); ν_{max}^{KBr} 3340, 3170, 1670, 1625, 1585, 1545, 1475, 1445, 1390, 1345, 1315, 1255, 1230, 1150, 1085, 1055, 940, 880, 870, 795, 770, 750, 665, 640 $cm.^{-1}$.

Anal. Calcd. for $C_8H_9N_2OCl$: C, 52.05; H, 4.92; N, 15.18. Found: C, 51.96; H, 4.97; N, 14.95.

Condensation of Tryptyl Bromide with the Amide 16.—A mixture of 2-chloro-4-carboxamido-5-ethylpyridine (190 mg.), tryptyl bromide (720 mg.) and dioxane (2 ml.) was heated for 44 hr. at 70–80°. The solution was concentrated and the red, crystalline product digested with a little methanol and cooled to yield 110 mg. of crystals which was recrystallized from methanol to give 100 mg. of pure product.

m.p. 312–315° dec.; λ_{max}^{EtOH} 220, 255, 320 and 400 mμ (ε 24,500, 11,100, 17,400 and 13,500, resp.); ν_{max}^{KBr} 1675, 1640, 1615, 1555, 1500, 1450, 1420, 1380, 1365, 1330, 1285, 1245, 1220, 1180, 1145, 1125, 1085, 1065, 900, 765, 750 cm.$^{-1}$.

Anal. Calcd. for $C_{18}H_{16}ON_2Br$: C, 58.07; H, 4.87; N, 11.29. Found: C, 58.25; H, 4.97; N, 11.22.

Dehydrogenation and Hydrolysis of the Condensation Product 17.—A solution of the condensation product (110 mg.) and tetrachloro-*o*-benzoquinone (460 mg.) in ethanol (10 ml.) was heated under reflux for 20 hr. and the solvent subsequently evaporated. Recrystallization of the residue from methanol–ethyl acetate yielded 85 mg. of a crystalline product which was heated under reflux for 1 day in methanol (5 ml.) and concentrated hydrochloric acid (4 ml.). The solution was concentrated and diluted with water to give 70 mg. of a crystalline hydrochloride salt which, after two recrystallizations from methanol–ethyl acetate, had m.p. 300–301° dec. pure and mixed with authentic flavocarpine hydrochloride (m.p. 301–302° dec.). (Conversion to flavocarpine seems to have occurred.) Its infrared spectrum was almost identical with that of authentic flavocarpine hydrochloride. The synthetic hydrochloride salt was converted to the acetate salt on a column of Rohm and Haas IR-4B anion exchange resin on the acetate cycle. Recrystallization of the crude product from glacial acetic acid gave a pure product, m.p. 306–307° pure, and mixed with authentic flavocarpine, m.p. 307–308°. The infrared spectra (in KBr) and the ultraviolet spectra (in 0.01 *N* hydrochloric acid in ethanol, in 0.01 *N* sodium hydroxide in ethanol and in ethanol) of the natural and synthetic products were identical.

7H-Pyrido-[2,3-c]-carbazole (8), $\lambda_{max}^{0.01\ N\ HCl-MeOH}$ 227, 252, 258, 303 and 391 mμ (ε 22,000, 30,500, 28,000, 20,000 and 8500); $\lambda_{max}^{0.01\ N\ NaOH-MeOH}$ 225, 245, 280 and 342 mμ (ε 27,000, 30,000, 32,000 and 9,000).

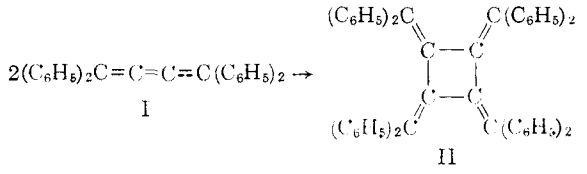
7H-Pyrido-[3,4-c]-carbazole (9), $\lambda_{max}^{0.01\ N\ HCl-MeOH}$ 232, 252, 295, 390 and 408 mμ (ε 21,000 33,000, 25,000, 8,000, 8,500); $\lambda_{max}^{0.01\ N\ NaOH-MeOH}$ 227, 238, 270, 283, 335, 362 and 375 mμ (ε 44,000, 38,000, 34,000, 23,000, 10,000, 9,000, 5,000).

COMMUNICATIONS TO THE EDITOR

THE PHOTODIMER OF TETRAPHENYLBUTATRIENE; DERIVATIVES OF TETRAMETHYLENECYCLOBUTANE

Sir:

Tetraphenylbutatriene (I) is dimerized[1] by solar irradiation in the solid state. It is now reported that the photodimer is tetrakis-(diphenylmethylene)-cyclobutane (II)[2] and thus is derived from

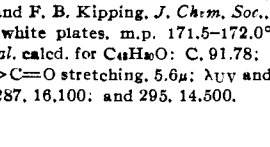


I II

center to center dimerization of I. The structure of II[3] is based on physical evidence and the structural assignments made for its ozonolysis and derived products. Photodimer II is a stable derivative of tetramethylenecyclobutane[4]; because of its simple preparation and the structures of its oxidation products, it also serves as a source of tetramethylenecyclobutanoid derivatives.

Photodimer II[5] is obtained preparatively by sunlamp irradiation (4–5 days) of I.[6] Its infrared absorption is similar to that of I with the exception of new absorption at 13.9μ; absorptions for allenic, acetylenic, or polysubstituted phenyl groups are absent. Photodimer II exhibits n.m.r. absorption for its phenyl groups only at ~ 3.0τ.[7] The shielding in II apparently stems from interactions of the phenyl groups which are prevented sterically from being totally coplanar. Partial conjugation in II is indicated, however, by its extensive ultraviolet absorption: $\lambda_{(CHCl_3)}$ 274 (ε = 18,300), λ_{max} 307–308 (ε = 39,500).[8]

Photodimer II decomposes to I on melting; it does not form adducts with maleic anhydride or tetracyanoethylene. Ozonolysis of II in chloroform yields benzophenone and tris-(diphenylmethylene)-cyclobutanone (III).[9] The n.m.r. of



III

the hydrogens (2.85 τ) in III indicates that there is less overlapping of the phenyl groups in III than in II. Monoketone III does not form a semicarbazone or a 2,4-dinitrophenylhydrazone even under forcing conditions; reduction of III, how-

(1) K. Brand, *Ber.*, **54**, 1947 (1921).

(2) From the Ph.D. dissertation of R. O. Uhler, The Ohio State University, 1960; R. O. Uhler and H. Shechter, 138th Meeting of American Chemical Society, New York, N. Y., Sept. 14, 1960, Abst. 70-P.

(3) The following head to head, head to tail, head to center, center to ends, and ends to ends photodimers (and their isomeric transannular derivatives) are discarded because they do not accommodate the experimental results: 1,2-bis-(diphenylvinylidene)-3,3,4,4-tetraphenylcyclobutane, 1,3-bis-(diphenylvinylidene)-2,2,4,4-tetraphenylcyclobutane, 1,2-bis-(diphenylmethylene)-3-diphenylvinylidene-4,4-diphenylcyclobutane, 4,5-bis-(diphenylmethylene)-3,3,6,6-tetraphenylcyclohexyne, and 3,3,4,4,7,7,8,8-octaphenyl-1,5-cyclooctadiyne.

(4) J. D. Roberts, A. Streitwieser, Jr., and C. M. Regan, *J. Am. Chem. Soc.*, **74**, 4579 (1952), predict that tetramethylenecyclobutane has considerable delocalization energy and exists in the singlet state.

(5) Yellow-green fluorescent crystals, m.p. (uncorr.) 290–293°, lit.[1] m.p. 280–281°; *anal.* calcd. for $C_{56}H_{44}$: C, 94.34; H, 5.66; mol. wt., 713. Found: C, 94.14; H, 5.47; mol. wt. (camphor), 695.

(6) J. Wolinski, *Roczniki Chem.*, **29**, 23 (1955).

(7) The n.m.r. absorption for the phenyl groups in tetraphenylbutatriene and other non-shielded derivatives occurs at ~2.68 τ. Shielded phenyl absorption has been observed[7c] at ~3.0 τ for *cis*-1,2-diphenylcyclobutanes; absorption is normal in *trans*-1,2- and *cis*-1,3-diphenylcyclobutanes (W. J. Link, Ph.D. dissertation, The Ohio State University (1960)).

(8) (a) 1,1-Diphenylethylene[8b] and 1,2-bis-(diphenylmethylene)-cyclobutane[8c] absorb at 250 (11,000)[8b] and 351 mμ (21,400).[8c] respectively; (b) E. A. Braude, *Ann. Rep. Progr. Chem.*, **42**, 105 (1945); (c) K. B. Alberman and F. B. Kipping, *J. Chem. Soc.*, 779 (1951).

(9) Polymorphs: white plates, m.p. 171.5–172.0°; white needles, m.p. 184.0–185°; *anal.* calcd. for $C_{44}H_{30}O$: C, 91.78; H, 5.37. Found: C, 91.54; H, 5.57. >C=O stretching, 5.6μ; λ_{UV} and ϵ_{UV} (95% methanol): 279, 16,300; 287, 16,100; and 295, 14,500.